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Short communication

Revisiting Acute Respiratory Distress Syndrome ventilation management: Time for a paradigm shift focusing on tidal volume

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ABSTRACT

Acute Respiratory Distress Syndrome (ARDS) remains a critical challenge in intensive care medicine, with persistently high mortality despite decades of research and advancements in supportive therapies. Mechanical ventilation, particularly low tidal volume (VT) strategies, has become the cornerstone of ARDS management; however, emerging evidence suggests that a uniform application of these approaches may not be universally beneficial. This viewpoint critically examines the evolution of ARDS ventilation strategies, from high VT methods to protective ventilation protocols centered on reduced VT and plateau pressures. It explores the limitations of current guidelines, highlighting how global parameters such as VT and driving pressure (ΔP) may inadequately capture the complex and heterogeneous pathophysiology of ARDS. Concepts like mechanical power, compliance-based ventilation, and transpulmonary pressure offer promising avenues for more personalized care but remain underutilized in clinical practice. Additionally, this viewpoint underscores the significance of heart-lung interactions and the impact of ventilator settings on cardiovascular function, further complicating one-size-fits-all approaches. Ultimately, this work calls for a reassessment of existing paradigms, advocating for individualized, physiology-driven strategies that move beyond population-based protocols to better address the nuanced needs of ARDS patients.

Acute Respiratory Distress Syndrome (ARDS) is characterized by severe hypoxemia, alveolar infiltrates due to increased permeability, and histological damage resulting from lung inflammation (ARDS Definition Task Force et al., 2012). ARDS continues to be a major challenge in critical care, with high mortality rates persisting despite advances in research and clinical strategies (Al-Husinat et al., 2025). It may be time to pause and reconsider whether the path we have been following for decades is truly the best one, or if returning to historical insights, possibly refining, could offer a new approach to managing ARDS. To date, treatment for ARDS remains largely supportive and mechanical ventilation is the cornerstone of supportive care for ARDS (Al-Husinat et al., 2025; Battaglini et al., 2021).

Many years ago, ARDS was managed using higher tidal volumes (V_T) (> 10 ml/kg of predicted body weight [PBW]) and elevated plateau pressures (P_{PLAT}) (> 40 cmH_2O) to normalize arterial blood gases (Marini, 1996). However, over the past two decades, a growing body of experimental and clinical evidence has consistently demonstrated that such ventilatory strategies contribute to ventilator-induced lung injury (VILI), exacerbating lung damage rather than improving outcomes (Slutsky and Ranieri, 2013).

The ARDS Network trial was pivotal in establishing a new approach to ventilation, revealing that, in contrast to traditional "high V_T" approaches, utilizing a "low V_T" of approximately 6 ml/kg PBW significantly reduced mortality from 40 % to 31 % (Acute Respiratory Distress Syndrome Network et al., 2000). This finding led to the widespread adoption of 6 ml/kg PBW as the standard V_T for managing ARDS. Despite current guidelines recommend using a V_T of 6–8 ml/kg PBW, it remains unclear whether this “protective” approach is universally beneficial for all patients. The trial focused on comparing two extremes but did not explore the intermediate values between these endpoints or below the threshold considered “protective.” This oversight leaves a gap in our understanding of the true benefit of this ventilatory strategy, especially for specific subgroups of ARDS patients. Notably, even with the implementation of “low V_T” strategies, many ARDS patients still

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display signs of lung hyperinflation, raising doubts as to whether these strategies are truly protective (Terragni et al., 2007). Indeed, in heterogeneous lungs, some areas may be severely affected while others remain relatively healthy. This uneven distribution can result in significant discrepancies in V_T delivery across different lung regions. For instance, areas of the lung that are less compliant may receive less ventilation, leading to underinflation, while more compliant regions may be overdistended, increasing the risk of VILI (Battaglini et al., 2023).

Furthermore, calibrating V_T to PBW may not be ideal, as it fails to account for the reduced ventilable lung tissue in ARDS patients (Goligher et al., 2021; Amato et al., 2015). An alternative approach may involve adjusting V_T according to the aerated portion of the lung, as estimated by respiratory system compliance (C_{RS}) (Amato et al., 2015).

The concept of driving pressure ($\Delta P = V_T/C_{RS}$) has gained attention as an accurate predictor of outcomes in ARDS patients. The beneficial effects of reduced V_T are largely mediated by a decrease in ΔP. Therefore, clinicians could aim to optimize ΔP and C_{RS}–the elastic components contributing to mechanical power and VILI–when setting V_T (Amato et al., 2015). Moreover, elevated plateau pressures can indicate areas of lung overdistension or reduced compliance, making it crucial to monitor and adjust ventilatory settings accordingly. However, it remains unclear whether ΔP is truly an indicator of unsafe V_T and whether it has a direct correlation to patient outcomes; similarly, it is unclear which factors influence C_{RS} and how the interaction between V_T and ΔP affects clinical outcomes (Pellegrini et al., 2024). A more recent study has reinforced these notions. The trial found that reducing ΔP below 15 cmH_2O and, more ideally, below 10 cmH_2O, resulted in significant reductions in 30-day ventilator mortality. Notably, these benefits were most pronounced when ΔP was minimized at the onset of mechanical ventilation and maintained over extended ventilation periods (Urner et al., 2023). In the STAMINA clinical trial involving patients with moderate to severe ARDS secondary to community-acquired pneumonia (CAP), a ΔP-limiting strategy, based on PEEP titration according to the best respiratory system compliance and tidal volume adjustment, while not resulting in an increase in the number of ventilator-free days at day 28 compared to a standard low-PEEP strategy, showed encouraging trends toward improved oxygenation, reduced markers of ventilator-induced lung injury, and improved lung mechanics in the ΔP-guided group (Maia et al., 2025). These findings underscore the importance of controlling ΔP, particularly in the early stages of mechanical ventilation. However, the variability in how ΔP interacts with clinical outcomes in ARDS heterogeneity remains poorly understood. There could be a finer line between "protective" and "excessive" ventilation that has yet to be fully explored.

An increasingly recognized dimension in the heterogeneity of ARDS is the identification of distinct biological phenotypes, particularly the hyperinflammatory and hypoinflammatory subtypes (Nasa et al., 2025). These phenotypes were consistently identified through post hoc latent class analysis of five randomized controlled trials (RCTs), based on clinical characteristics and blood biomarkers linked to coagulopathy, endothelial injury, and inflammation (Calfee et al., 2014, 2018; Famous et al., 2017; Sinha et al., 2018; Delucchi et al., 2018). The hyperinflammatory phenotype is characterized by elevated plasma levels of pro-inflammatory cytokines (such as TNF-α, IL-6 and IL-8), increased markers of endothelial damage, more severe shock, higher prevalence of metabolic acidosis, and significantly higher mortality compared to the hypoinflammatory phenotype. Crucially, these phenotypes exhibit differential responses to ventilatory strategies, fluid management and pharmacological interventions. The hyperinflammatory phenotype appears to benefit more from higher levels of PEEP and conservative fluid management strategies. Similarly, this subgroup appears more likely to benefit from immunomodulatory therapies, including corticosteroids, potentially due to their heightened inflammatory milieu. In contrast, patients with the hypoinflammatory phenotype may not respond favorably to such interventions and could even be harmed by them—for instance, overly aggressive PEEP settings may contribute to lung overdistension in patients with less recruitable lung tissue and lower systemic inflammation (Calfee et al., 2014, 2018; Famous et al., 2017; Sinha et al., 2018; Delucchi et al., 2018). Therefore, the recognition of biological subphenotypes of ARDS offers a promising avenue toward personalized medicine, in which the identification of biologically distinct subgroups allows for therapeutic strategies to be tailored.

Mechanical power (MP), the energy delivered to the lungs per unit time during mechanical ventilation, has emerged as a strategy to reduce the incidence of ventilator-induced lung injury (VILI) and improve outcomes for patients with ARDS (Gattinoni et al., 2016). Expressed in Joules per minute (J/min), MP integrates V_T, respiratory rate, and inspiratory pressure into a single metric, allowing clinicians to assess the total energy delivered to the lungs over time. Various mathematical formulas have been proposed for bedside application (Gattinoni et al., 2016; Giosa et al., 2019; Becher et al., 2019). As V_T increases, MP also increases, provided other factors (like respiratory rate and inspiratory pressure) remain constant. Higher V_T contributes to increased energy delivery per breath, which can enhance ventilation efficiency. In critically ill patients, MP > 17 J/min is linked to higher mortality (Serpa Neto et al., 2018), while MP > 22 J/min correlates with increased 3-year and 28-day mortality in ARDS patients (Parhar et al., 2019). An experimental study found that MP values exceeding 25 J/min caused more severe lung damage (Cressoni et al., 2016). Additionally, in ECMO patients, MP > 14.4 J/min in the first 3 days was the only ventilatory parameter independently associated with 90-day hospital mortality (Chiu et al., 2021). However, the clinical utility of MP remains uncertain due to challenges in measurement and interpretation.

Another notable parameter is the formula proposed by Costa and colleagues: (4 × ΔP) + RR. This formula has shown a significant association with mortality and poor neurological outcomes, outperforming mechanical power (MP) in patients post-cardiac arrest without ARDS (Costa et al., 2021). Recent studies indicate that this composite formula, calculated as (4 × ΔP) + RR, is independently linked to mortality and poor neurological outcomes at 6 months. This highlights the importance of ventilator settings, specifically ΔP and respiratory rate (RR), in the first 3 days after cardiac arrest (Robba et al., 2022). V_T is indirectly related to both ΔP and RR, as variations in V_T can influence ΔP. Thus, optimizing V_T along with ΔP and RR may further enhance patient outcomes, warranting additional research to explore its implications in ARDS patients.

In the context of personalized medicine, one of the most striking gaps in current ARDS management is the lack of widespread adoption of esophageal pressure (Pes) measurements to estimate transpulmonary pressure (Ptp), a direct measure of lung stress (Akoumianaki et al., 2014). The Lung Safe study revealed that less than 1 % of ARDS patients had this parameter measured, despite its potential to provide critical insights into pulmonary mechanics (Bellani et al., 2016). After all these years, this simple yet crucial metric has not been more widely adopted. The complexity of implementing esophageal pressure measurement in routine clinical practice, combined with a focus on global ventilator parameters like V_T and ΔP, may explain its limited use. However, focusing on lung mechanics through direct Ptp measurements may be critical to reducing VILI and improving patient outcomes (Pelosi et al., 2021).

Although landmark studies have established valuable benchmarks for ventilation settings, we must ask whether a “one-size-fits-all” approach is truly the most effective strategy for every ARDS patient. Perhaps the time has come to adopt a more personalized approach, more in tune with the pathophysiological state of the individual patient than with population-based evidence. Current evidence suggests that factors such as ΔP and C_{RS} should be considered when determining optimal ventilatory settings (Goligher et al., 2021). However, these parameters are global metrics and do not account for the regional behavior of lung tissue; alveolar recruitment and overdistension reflect the heterogeneous respiratory mechanics of ARDS patients. Tidal recruitment is a

common occurrence in ARDS patients, especially at low PEEP. It refers to the cyclic process of alveolar units opening and closing during tidal ventilation. When this occurs, alveolar units that are collapsed at end-expiration reopen due to the increase in airway pressure resulting from V_T inflation. C_{RS} is the sum of the compliances of all alveolar units that are open at end-inspiration. When a collapsed alveolar unit reopens during inspiration, as happens with tidal recruitment, its individual compliance tends toward infinity. This finally increases static C_{RS}. This explains why tidal recruitment leads to very high static compliance at low PEEP and why increasing PEEP, which limits tidal recruitment, may lead to a deterioration in compliance, even in the presence of significant recruitment (Grieco et al., 2022).

The complexity of ARDS and the variability in its presentation across different patient populations make it clear that what works for one patient may not work for another. Tailoring ventilation strategies to the physiological needs of the individual, rather than sticking to generalized standards, could lead to better outcomes.

In this regard, prone positioning and electrical impedance tomography (EIT)-tailored ventilation strategies deserve mention. Prone positioning improves lung homogeneity in ARDS by reducing gravitational atelectasis promoted by the supine position. Edema and compression by the heart and abdominal viscera, by increasing lung weight, further aggravate dorsal lung collapse, resulting in preferential distribution of V_T toward the ventral regions of the lung and increasing the risk of lung overdistension due to higher Ptp. In addition, lung perfusion is preferentially distributed toward the dorsal regions, compromising ventilation-perfusion matching and increasing intrapulmonary shunting (Pelosi et al., 2002; Guérin et al., 2020; Swenson and Swenson, 2021). Prone positioning mitigates these effects by promoting more homogeneous ventilation (Gattinoni et al., 2013a, 2013b; Wang et al., 2022; Scholten et al., 2017). Evidence indicates improved outcomes in ARDS patients, particularly those with heterogeneous lung injury. The PROSEVA multicenter randomized controlled trial demonstrated that placing patients with severe ARDS in the prone position for at least 16 h per day significantly reduced mortality by approximately 17 % compared to the semi-recumbent supine position, despite both groups receiving identical lung-protective mechanical ventilation strategies (Guérin et al., 2013). A subsequent meta-analysis of eight RCTs confirmed reduced mortality with prone positioning applied for $\geq$ 12 h per day in severe ARDS (Munshi et al., 2017).

Electrical Impedance Tomography (EIT) is a non-invasive bedside tool that provides real-time lung impedance data, reflecting lung volume changes (Jimenez et al., 2022). It helps detect and measure regional alveolar overdistention and collapse, supporting personalized PEEP titration (Costa et al., 2009; Frerichs et al., 2017).

A recent RCT showed that EIT-guided PEEP titration decoupled PEEP from FiO_2 settings but did not improve long-term outcomes compared to conventional PEEP/FiO_2 tables (He et al., 2021). Another trial found EIT-guided PEEP led to lower PEEP levels and improved survival than pressure-volume loop-based settings (Hsu et al., 2021). A randomized crossover study also reported reduced mean pulmonary artery pressure with EIT-guided PEEP compared to High-PEEP/FiO_2 strategy in moderate-to-severe ARDS patients (Jimenez et al., 2023). However, EIT use in ARDS is limited by high device costs, need for specialized training, and the critical requirement for accurate electrode belt placement to ensure data reliability.

Furthermore, the multisystem impact of ARDS and mechanical ventilation, particularly the heart-lung interaction, cannot be overlooked. The interaction between the heart and lungs is a key aspect of ARDS ventilation management. This interaction is influenced by the anatomy of the thoracic cavity and the vascular connections between the heart and lungs. Respiratory cycles affect intrathoracic pressure (ITP), which in turn influences cardiac pressures. During inspiration, decreased pleural pressure lowers right atrial pressure (Pra), enhancing venous return and increasing right ventricular (RV) stroke volume. Conversely, during expiration, rising pleural pressure increases Pra, reducing venous return and RV stroke volume (Grübler et al., 2017; Mahmood and Pinsky, 2018). Mechanical ventilation alters these dynamics; positive pressure ventilation with increasing V_T raises ITP, potentially decreasing venous return and RV preload, which may lead to reduced cardiac output and hypotension (Marini et al., 1981; Corp et al., 2021). This effect is more pronounced in severe ARDS, where mechanical ventilation can increase pulmonary vascular resistance (PVR) and worsen RV dysfunction (Walkey et al., 2017; McGuigan et al., 2024). Additionally, PEEP elevates ITP, further reducing venous return and complicating management, with effects influenced by the balance between alveolar recruitment and overdistension in ARDS patients (Fig. 1) (Ganeriwal et al., 2023; Joseph et al., 2024; Battaglini et al., 2024). Furthermore, strategies like esophageal pressure monitoring can help fine-tune ventilation to minimize adverse cardiovascular effects (Bonatti et al., 2019). Ventilatory settings, such as V_T and PEEP, need to be carefully adjusted, especially in patients with obesity, where chest wall compliance affects pressure transmission. Managing these heart-lung interactions is critical for optimizing patient outcomes in ARDS, as improper ventilation can lead to worsened lung injury or cardiovascular compromise (Silva et al., 2022; Rocha et al., 2024).

Finally, the evolving landscape of ARDS research is increasingly shaped by adaptive platform trials such as INCEPT, PRACTICAL, PANTHER, I-SPY, TRAITS and REMAP-CAP. These innovative trial designs allow for the simultaneous evaluation of multiple interventions within a single, flexible framework. By streamlining data collection and accelerating hypothesis testing, these platforms offer a dynamic method for generating high-quality evidence while adapting to emerging insights. Their collaborative and patient-centered approach holds the promise of advancing precision medicine in ARDS, bridging the gap between bench research and bedside application more efficiently than traditional RCTs.

Take-home message

Over time the landscape of ARDS management has evolved but has not necessarily progressed in the way we might have hoped. The high mortality rate remains a significant problem, and while technological and methodological advancements have certainly improved some aspects of care, they have not solved the fundamental issue of ARDS treatment. Perhaps, after decades of following the same basic principles, it is time to ask whether a fundamental shift is necessary. Should we adopt more individualized, physiologically based approaches such as transpulmonary pressure and regional ventilation, rather than focusing primarily on global parameters such as V_T and ΔP? Or should we continue to refine the existing standards, exploring intermediate values of V_T and ΔP that might offer a more nuanced approach to ventilation?

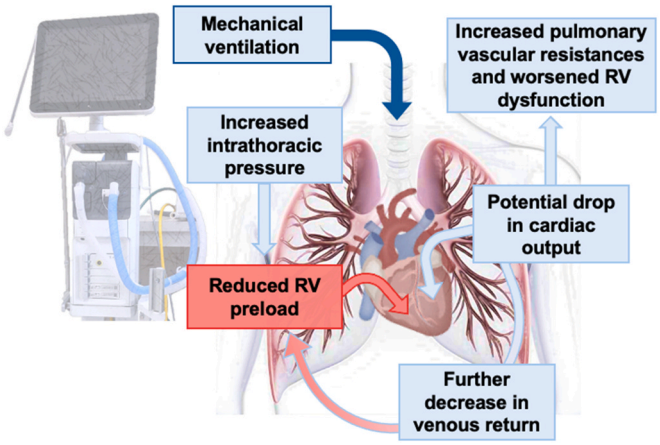
Mechanical ventilation
Increased pulmonary vascular resistances and worsened RV dysfunction
Increased intrathoracic pressure
Potential drop in cardiac output
Reduced RV preload
Further decrease in venous return

Fig. 1. Heart-lungs interactions during mechanical ventilation in acute respiratory distress syndrome. RV: Right Ventricle.

These questions remain open, but the time has come to re-evaluate our approach.

CRediT authorship contribution statement

Maria Vargas: Writing – review & editing, Visualization, Validation, Supervision, Project administration, Methodology, Investigation. **Denise Battaglini:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation. **Raffaele Merola:** Writing – original draft, Visualization, Validation, Project administration, Methodology, Investigation, Conceptualization.

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Conflict of Interest

The authors declare that they have no competing interests.

Declaration of Competing Interest

I have nothing to declare.

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References

Acute Respiratory Distress Syndrome Network, Brower, R.G., Matthay, M.A., Morris, A., Schoenfeld, D., Thompson, B.T., Wheeler, A., 2000. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N. Engl. J. Med. 342 (18), 1301–1308.

Akoumianaki E., Maggiore S.M., Valenza F., Bellani G., Jubran A., Loring S.H., Pelosi P., Talmor D., Grasso S., Chiumello D., Guérin C., Patroniti N., Ranieri V.M., Gattinoni L., Nava S., Terragni P.P., Pesenti A., Tobin M., Mancebo J., Brochard L., PLUG Working Group (Acute Respiratory Failure Section of the European Society of Intensive Care Medicine), 2014. The application of esophageal pressure measurement in patients with respiratory failure. Am. J. Respir. Crit. Care Med. vol. 189(no. 5), pp. 520–31.

Al-Husinat, L., Azzam, S., Al Sharie, S., Araydah, M., Battaglini, D., Abushehab, S., Cortes-Puentes, G.A., Schultz, M.J., Rocco, P.R.M., 2025. A narrative review on the future of ARDS: evolving definitions, pathophysiology, and tailored management. Crit. Care 29 (1), 88.

Amato, M.B., Meade, M.O., Slutsky, A.S., Brochard, L., Costa, E.L., Schoenfeld, D.A., Stewart, T.E., Briel, M., Talmor, D., Mercat, A., Richard, J.C., Carvalho, C.R., Brower, R.G., 2015. Driving pressure and survival in the acute respiratory distress syndrome. N. Engl. J. Med. 372 (8), 747–755.

ARDS Definition Task Force, Ranieri, V.M., Rubenfeld, G.D., Thompson, B.T., Ferguson, N.D., Caldwell, E., Fan, E., Camporota, L., Slutsky, A.S., 2012. Acute respiratory distress syndrome: the Berlin Definition. JAMA 307 (23), 2526–2533.

Battaglini, D., Sottano, M., Ball, L., Robba, C., Rocco, P.R.M., Pelosi, P., 2021. Ten golden rules for individualized mechanical ventilation in acute respiratory distress syndrome. J. Intensive Med. 1 (1), 42–51.

Battaglini, D., Fazzini, B., Silva, P.L., Cruz, F.F., Ball, L., Robba, C., Rocco, P.R.M., Pelosi, P., 2023. Challenges in ARDS definition, management, and identification of effective personalized therapies. J. Clin. Med. 12 (4), 1381.

Battaglini, D., Roca, O., Ferrer, R., 2024. Positive end-expiratory pressure optimization in ARDS: physiological evidence, bedside methods and clinical applications. Intensive Care Med. 50 (5), 762–765.

Becher, T., van der Staay, M., Schädler, D., Frerichs, I., Weiler, N., 2019. Calculation of mechanical power for pressure-controlled ventilation. Intensive Care Med. 45 (9), 1321–1323.

Bellani, G., Laffey, J.G., Pham, T., Fan, E., Brochard, L., Esteban, A., Gattinoni, L., van Haren, F., Larsson, A., McAuley, D.F., Ranieri, M., Rubenfeld, G., Thompson, B.T., Wrigge, H., Slutsky, A.S., Pesenti, A., LUNG SAFE Investigators, ESICM Trials Group, 2016. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. JAMA 315 (8), 788–800.

Bonatti, G., Robba, C., Ball, L., Silva, P.L., Rocco, P.R.M., Pelosi, P., 2019. Controversies when using mechanical ventilation in obese patients with and without acute distress respiratory syndrome. Expert Rev. Respir. Med. 13 (5), 471–479.

Calfee, C.S., Delucchi, K., Parsons, P.E., Thompson, B.T., Ware, L.B., Matthay, M.A., NHLBI ARDS Network, 2014. Subphenotypes in acute respiratory distress syndrome: latent class analysis of data from two randomised controlled trials. Lancet Respir. Med. 2 (8), 611–620.

Calfee, C.S., Delucchi, K.L., Sinha, P., Matthay, M.A., Hackett, J., Shankar-Hari, M., McDowell, C., Laffey, J.G., O'Kane, C.M., McAuley, D.F., Irish Critical Care Trials Group, 2018. Acute respiratory distress syndrome subphenotypes and differential response to simvastatin: secondary analysis of a randomised controlled trial. Lancet. Respir. Med. 6 (9), 691–698.

Chiu, L.C., Lin, S.W., Chuang, L.P., Li, H.H., Liu, P.H., Tsai, F.C., Chang, C.H., Hung, C.Y., Lee, C.S., Leu, S.W., Hu, H.C., Huang, C.C., Wu, H.P., Kao, K.C., 2021. Mechanical power during extracorporeal membrane oxygenation and hospital mortality in patients with acute respiratory distress syndrome. Crit. Care 25 (1), 13.

Corp, A., Thomas, C., Adlam, M., 2021. The cardiovascular effects of positive pressure ventilation. BJA Educ. 21 (6), 202–209.

Costa, E.L., Borges, J.B., Melo, A., Suarez-Sipmann, F., Toufen, C., Jr, Bohm, S.H., Amato, M.B., 2009. Bedside estimation of recruitable alve-olar collapse and hyperdistension by electrical impedance tomography. Intensive Care Med. 35 (6), 1132–1137.

Costa, E.L.V., Slutsky, A.S., Brochard, L.J., Brower, R., Serpa-Neto, A., Cavalcanti, A.B., Mercat, A., Meade, M., Morais, C.C.A., Goligher, E., Carvalho, C.R.R., Amato, M.B.P., 2021. Ventilatory variables and mechanical power in patients with acute respiratory distress syndrome. Am. J. Respir. Crit. Care Med. 204 (3), 303–311.

Cressoni, M., Gotti, M., Chiurazzi, C., Massari, D., Algieri, I., Amini, M., Cammaroto, A., Brioni, M., Montaruli, C., Nikolla, K., Guanziroli, M., Dondossola, D., Gatti, S., Valerio, V., Vergani, G.L., Pugni, P., Cadringher, P., Gagliano, N., Gattinoni, L., 2016. Mechanical power and development of ventilator-induced lung injury. Anesthesiology 124 (5), 1100–1108.

Delucchi, K., Famous, K.R., Ware, L.B., Parsons, P.E., Thompson, B.T., Calfee, C.S., ARDS Network, 2018. Stability of ARDS subphenotypes over time in two randomised controlled trials. Thorax 73 (5), 439–445.

Famous, K.R., Delucchi, K., Ware, L.B., Kangelaris, K.N., Liu, K.D., Thompson, B.T., Calfee, C.S., ARDS Network, 2017. Acute respiratory distress syndrome subphenotypes respond differently to randomized fluid management strategy. Am. J. Respir. Crit. Care Med. 195 (3), 331–338.

Frerichs, I., Amato, M.B., van Kaam, A.H., Tingay, D.G., Zhao, Z., Grychtol, B., Bodenstein, M., Gagnon, H., Böhm, S.H., Teschner, E., Stenqvist, O., Mauri, T., Torsani, V., Camporota, L., Schibler, A., Wolf, G.K., Gommers, D., Leonhardt, S., Adler, A., TREND study group, 2017. Chest electrical impedance tomography examination, data analysis, terminology, clinical use and recommendations: consensus statement of the TRanslational EIT developmeNt stuDy group. Thorax 72 (1), 83–93.

Ganeriwal, S., Alves Dos Anjos, G., Schleicher, M., Hockstein, M.A., Tonelli, A.R., Duggal, A., Siuba, M.T., 2023. Right ventricle-specific therapies in acute respiratory distress syndrome: a scoping review. Crit. Care 27 (1), 104.

Gattinoni, L., Pesenti, A., Carlesso, E., 2013a. Body position changes redistribute lung computed-tomographic density in patients with acute respiratory failure: impact and clinical fallout through the following 20 years. Intensive Care Med. 39 (11), 1909–1915.

Gattinoni, L., Taccone, P., Carlesso, E., Marini, J.J., 2013b. Prone position in acute respiratory distress syndrome. Rationale, indications, and limits. Am. J. Respir. Crit. Care Med. 188 (11), 1286–1293.

Gattinoni, L., Tonetti, T., Cressoni, M., Cadringher, P., Herrmann, P., Moerer, O., Protti, A., Gotti, M., Chiurazzi, C., Carlesso, E., Chiumello, D., Quintel, M., 2016. Ventilator-related causes of lung injury: the mechanical power. Intensive Care Med. 42 (10), 1567–1575.

Giosa, L., Busana, M., Pasticci, I., Bonifazi, M., Macrì, M.M., Romitti, F., Vassalli, F., Chiumello, D., Quintel, M., Marini, J.J., Gattinoni, L., 2019. Mechanical power at a glance: a simple surrogate for volume-controlled ventilation. Intensive Care Med. Exp. 7 (1), 61.

Goligher, E.C., Costa, E.L.V., Yarnell, C.J., Brochard, L.J., Stewart, T.E., Tomlinson, G., Brower, R.G., Slutsky, A.S., Amato, M.P.B., 2021. Effect of lowering Vt on mortality in acute respiratory distress syndrome varies with respiratory system elastance. Am. J. Respir. Crit. Care Med. 203 (11), 1378–1385.

Grieco, D.L., Bongiovanni, F., Dell'Anna, A.M., Antonelli, M., 2022. Why compliance and driving pressure may be inappropriate targets for PEEP setting during ARDS. Crit. Care 26 (1), 234.

Grübler, M.R., Wigger, O., Berger, D., Blöchlinger, S., 2017. Basic concepts of heart-lung interactions during mechanical ventilation. Swiss Med. Wkly. 147, w14491.

Guérin, C., Reignier, J., Richard, J.C., Beuret, P., Gacouin, A., Boulain, T., Mercier, E., Badet, M., Mercat, A., Baudin, O., Clavel, M., Chatellier, D., Jaber, S., Rosselli, S., Mancebo, J., Sirodot, M., Hilbert, G., Bengler, C., Richecoeur, J., Gainnier, M., Bayle, F., Bourdin, G., Leray, V., Girard, R., Baboi, L., Ayzac, L., PROSEVA Study Group, 2013. Prone positioning in severe acute respiratory distress syndrome. N. Engl. J. Med. 368 (23), 2159–2168.

Guérin, C., Albert, R.K., Beitler, J., Gattinoni, L., Jaber, S., Marini, J.J., Munshi, L., Papazian, L., Pesenti, A., Vieillard-Baron, A., Mancebo, J., 2020. Prone position in ARDS patients: why, when, how and for whom. Intensive Care Med. 46 (12), 2385–2396.

He, H., Chi, Y., Yang, Y., Yuan, S., Long, Y., Zhao, P., Frerichs, I., Fu, F., Möller, K., Zhao, Z., 2021. Early individualized positive end-expiratory pressure guided by electrical impedance tomography in acute respiratory distress syndrome: a randomized con-trolled clinical trial. Crit. Care 25 (1), 230.

Hsu, H.J., Chang, H.T., Zhao, Z., Wang, P.H., Zhang, J.H., Chen, Y.S., Frerichs, I., Möller, K., Fu, F., Hsu, H.S., Chuang, S.P., Hsia, H.Y., Yen, D.H., 2021. Positive end-expiratory pressure titration with electrical impedance tomography and pressure-volume curve: a randomized trial in moderate to severe ARDS. Physiol. Meas. 42 (1), 014002.

Jimenez, J.V., Weirauch, A.J., Culter, C.A., Choi, P.J., Hyzy, R.C., 2022. Electrical impedance tomography in acute respiratory distress syndrome management. Crit. Care Med. 50 (8), 1210–1223.
Jimenez, J.V., Munroe, E., Weirauch, A.J., Fiorino, K., Culter, C.A., Nelson, K., Labaki, W. W., Choi, P.J., Co, I., Standiford, T.J., Prescott, H.C., Hyzy, R.C., 2023. Electric impedance tomography-guided PEEP titration reduces mechanical power in ARDS: a randomized crossover pilot trial. Crit. Care 27 (1), 21.
Joseph, A., Petit, M., Vieillard-Baron, A., 2024. Hemodynamic effects of positive end-expiratory pressure. Curr. Opin. Crit. Care 30 (1), 10–19.
Mahmood, S.S., Pinsky, M.R., 2018. Heart-lung interactions during mechanical ventilation: the basics. Ann. Transl. Med. 6 (18), 349.
Maia, I.S., Cavalcanti, A.B., Tramujas, L., Veiga, V.C., Oliveira, J.S., Sady, E.R.R., Barbante, L.G., Nicola, M.L., Gurgel, R.M., Damiani, L.P., Negrelli, K.L., Miranda, T. A., Laranjeira, L.N., Tomazzini, B., Zandonai, C., Pincelli, M.P., Westphal, G.A., Fernandes, R.P., Figueiredo, R., Sartori Bustamante, C.L., Norbin, L.F., Boschi, E., Lessa, R., Romano, M.P., Miura, M.C., Soares de Alencar Filho, M., Cés de Souza Dantas, V., Barreto, P.A., Hernandes, M.E., Grion, C., Laranjeira, A.S., Mezzaroba, A. L., Bahl, M., Starke, A.C., Biondi, R., Dal-Pizzol, F., Caser, E., Thompson, M.M., Padial, A.A., Leite, R.T., Araújo, G., Guimarães, M., Aquino, P., Lacerda, F., Hoffmann Filho, C.R., Melro, L., Pacheco, E., Ospina-Táscon, G., Ferreira, J.C., Calado Freires, F.J., Machado, F.R., Zampieri, F.G., BRICNet, 2025. Effect of a driving pressure-limiting strategy for patients with acute respiratory distress syndrome secondary to community-acquired pneumonia: the STAMINA randomised clinical trial. Br. J. Anaesth. 134 (3), 693–702.
Marini, J.J., 1996. Evolving concepts in the ventilatory management of acute respiratory distress syndrome. Clin. Chest Med. 17 (3), 555–575.
Marini, J.J., Culver, B.H., Butler, J., 1981. Mechanical effect of lung distention with positive pressure on cardiac function. Am. Rev. Respir. Dis. 124 (4), 382–386.
McGuigan, P.J., Bowcock, E.M., Barrett, N.A., Blackwood, B., Boyle, A.J., Cadamy, A.J., Camporota, L., Conlon, J., Cove, M.E., Gillies, M.A., McDowell, C., McNamee, J.J., O'Kane, C.M., Puxty, A., Sim, M., Parsons-Simmonds, R., Szakmany, T., Young, N., Orde, S., McAuley, D.F., 2024. The effect of lower tidal volume ventilation facilitated by extracorporeal carbon dioxide removal compared with conventional lung protective ventilation on cardiac function. Crit. Care Explor. 6 (1), e1028.
Munshi, L., Del Sorbo, L., Adhikari, N.K.J., Hodgson, C.L., Wunsch, H., Meade, M.O., Uleryk, E., Mancebo, J., Pesenti, A., Ranieri, V.M., Fan, E., 2017. Prone position for acute respiratory distress syndrome. a systematic review and meta-analysis. Ann. Am. Thorac. Soc. 14 (Suppl_4), S280–S288.
Nasa, P., Bos, L.D., Estenssoro, E., van Haren, F.M.P., Neto, A.S., Rocco, P.R.M., Slutsky, A.S., Schultz, M.J., investigators, D.I.O.S., 2025. Defining and subphenotyping ARDS: insights from an international Delphi expert panel. Lancet Respir. Med. S2213-2600(25)00115-S2218.
Parhar, K.K.S., Zjadewicz, K., Soo, A., Sutton, A., Zjadewicz, M., Doig, L., Lam, C., Ferland, A., Niven, D.J., Fiest, K.M., Stelfox, H.T., Doig, C.J., 2019. Epidemiology, mechanical power, and 3-year outcomes in acute respiratory distress syndrome patients using standardized screening. An observational cohort study. Ann. Am. Thorac. Soc. 16 (10), 1263–1272.
Pellegrini, M., Del Sorbo, L., Ranieri, V.M., 2024. Finding the optimal tidal volume in acute respiratory distress syndrome. Intensive Care Med. 50 (7), 1154–1156.
Pelosi, P., Brazzi, L., Gattinoni, L., 2002. Prone position in acute respiratory distress syndrome. Eur. Respir. J. 20 (4), 1017–1028.
Pelosi, P., Ball, L., Barbas, C.S.V., Bellomo, R., Burns, K.E.A., Einav, S., Gattinoni, L., Laffey, J.G., Marini, J.J., Myatra, S.N., Schultz, M.J., Teboul, J.L., Rocco, P.R.M., 2021. Personalized mechanical ventilation in acute respiratory distress syndrome. Crit. Care 25 (1), 250.
Robba, C., Badenes, R., Battaglini, D., Ball, L., Brunetti, I., Jakobsen, J.C., Lilja, G., Friberg, H., Wendel-Garcia, P.D., Young, P.J., Eastwood, G., Chew, M.S., Unden, J., Thomas, M., Joannidis, M., Nichol, A., Lundin, A., Hollenberg, J., Hammond, N., Saxena, M., Annborn, M., Solar, M., Taccone, F.S., Dankiewicz, J., Nielsen, N., Pelosi, P., TTM2 Trial Collaborators, 2022. Ventilatory settings in the initial 72h and their association with outcome in out-of-hospital cardiac arrest patients: a preplanned secondary analysis of the targeted hypothermia versus targeted normothermia after out-of-hospital cardiac arrest (TTM2) trial. Intensive Care Med. 48 (8), 1024–1038.
Rocha, N.N., Silva, P.L., Battaglini, D., Rocco, P.R.M., 2024. Heart-lung crosstalk in acute respiratory distress syndrome. Front. Physiol. 15, 1478514.
Scholten, E.L., Beitler, J.R., Prisk, G.K., Malhotra, A., 2017. Treatment of ARDS with prone positioning. Chest 151 (1), 215–224.
Serpa Neto, A., Deliberato, R.O., Johnson, A.E.W., Bos, L.D., Amorim, P., Pereira, S.M., Cazati, D.C., Cordioli, R.L., Correa, T.D., Pollard, T.J., Schettino, G.P.P., Timenetsky, K.T., Celi, L.A., Pelosi, P., Gama de Abreu, M., Schultz, M.J., PROVE Network Investigators, 2018. Mechanical power of ventilation is associated with mortality in critically ill patients: an analysis of patients in two observational cohorts. Intensive Care Med. 44 (11), 1914–1922.
Silva, P.L., Ball, L., Rocco, P.R.M., Pelosi, P., 2022. Physiological and pathophysiological consequences of mechanical ventilation. Semin. Respir. Crit. Care Med. 43 (3), 321–334.
Sinha, P., Delucchi, K.L., Thompson, B.T., McAuley, D.F., Matthay, M.A., Calfee, C.S., NHLBI ARDS Network, 2018. Latent class analysis of ARDS subphenotypes: a secondary analysis of the statins for acutely injured lungs from sepsis (SAILS) study. Intensive Care Med. 44 (11), 1859–1869.
Slutsky, A.S., Ranieri, V.M., 2013. Ventilator-induced lung injury. N. Engl. J. Med. 369 (22), 2126–2136.
Swenson, K.E., Swenson, E.R., 2021. Pathophysiology of acute respiratory distress syndrome and COVID-19 lung injury. Crit. Care Clin. 37 (4), 749–776.
Terragni, P.P., Rosboch, G., Tealdi, A., Corno, E., Menaldo, E., Davini, O., Gandini, G., Herrmann, P., Mascia, L., Quintel, M., Slutsky, A.S., Gattinoni, L., Ranieri, V.M., 2007. Tidal hyperinflation during low tidal volume ventilation in acute respiratory distress syndrome. Am. J. Respir. Crit. Care Med. 175 (2), 160–166.
Urner, M., Jüni, P., Rojas-Saunero, L.P., Hansen, B., Brochard, L.J., Ferguson, N.D., Fan, E., 2023. Limiting dynamic driving pressure in patients requiring mechanical ventilation. Crit. Care Med. 51 (7), 861–871.
Walkey, A.J., Goligher, E.C., Del Sorbo, L., Hodgson, C.L., Adhikari, N.K.J., Wunsch, H., Meade, M.O., Uleryk, E., Hess, D., Talmor, D.S., Thompson, B.T., Brower, R.G., Fan, E., 2017. Low tidal volume versus non-volume-limited strategies for patients with acute respiratory distress syndrome. A systematic review and meta-analysis. Ann. Am. Thorac. Soc. 14 (Suppl_4), S271–S279.
Wang, Y.X., Zhong, M., Dong, M.H., Song, J.Q., Zheng, Y.J., Wu, W., Tao, J.L., Zhu, L., Zheng, X., 2022. Prone positioning improves ventila-tion-perfusion matching assessed by electrical impedance tomography in patients with ARDS: a prospective physiological study. Crit. Care 26 (1), 154.